



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Parce *et al.*

Appl. No.: 09/721,508

Filed: November 22, 2000

For: **High Throughput Screening Assay
Systems in Microscale Fluidic
Devices**

Confirmation No.: 5229

Art Unit: 1639

Examiner: Tran, My Chau T.

Atty. Docket: 2052.0020006/LEA/EDH

Brief on Appeal Under 37 C.F.R. § 1.194

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

A Notice of Appeal from the final rejection of claims 78, 81, and 87 for the above captioned U.S. patent application was filed on August 12, 2003. Appellants hereby file this Appeal Brief in triplicate, together with the required brief filing fee of \$320.00 under 37 C.F.R. § 1.17(c).

Appellants have filed concurrently with this Appeal Brief a Request for an Oral Hearing under 37 C.F.R. § 1.194. The required fee of \$280.00 under 37 C.F.R. § 1.17(d) has been paid together with the brief filing.

The Commissioner is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19 0036.

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I. Real Party in Interest (37 C.F.R. § 1.192(c)(1))

The real party in interest in this appeal is Caliper Technologies Corp. ("Caliper"), 605 Fairchild Drive, Mountain View, California 94043-2234. An assignment assigning all right, title and interest in and to the patent application from the inventors to Caliper was recorded in the U.S. Patent & Trademark Office (USPTO) in parent Appl. No. 08/671,987 on June 28, 1996 at Reel 9029, Frame 0054.

II. Related Appeals and Interferences (37 C.F.R. § 1.192(c)(2))

There are no appeals or interferences related to the above-captioned application which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

III. Status of the Claims (37 C.F.R. § 1.192(c)(3))

This application was filed on November 22, 2000 and assigned U.S. Application No. 09/721,508 ("508 application"). The '508 application included claims 1-74. At the time of filing the application, a Preliminary Amendment was filed that cancelled claims 1-74 and added new claims 75-90. Notice was also provided at that time to the USPTO that claims 75-90 were copied from U.S. Patent No. 6,103,199 in an effort to provoke an interference.

In a Supplemental Amendment and Reply filed on October 28, 2002, new claims 91-107 were also added. In an Office Action dated February 12, 2003 (Paper No. 18), claims 91-107 were withdrawn from consideration as being directed to a non-elected invention. As such, claims 75-107 are now pending in the present application. As noted below, Appellants have submitted herewith an amendment to cancel the non-elected claims 91-107.

Claims 75-77, 79, 80, 82-86 and 88-90 were allowed in an Office Action mailed July 2, 2002. Of these, claims 75, 76, and 83 are independent. Claims 78, 81, and 87 were rejected. In an Office Action mailed February 12, 2003, claims 78, 81, and 87 were finally rejected.

Appellants submit herewith, in a separate paper, an Amendment to cancel non-elected claims 91-107 from the present application pursuant to MPEP § 1207. This Amendment conforms to the requirements of 37 C.F.R. § 1.116 in that it does not raise new issues for search. Upon entry of this Amendment, claims 75-90 will be pending in the present application ("the pending claims").

A Notice of Appeal was filed on August 12, 2003. Claims 78, 81, and 87 are on appeal. A copy of the claims on appeal, and the claims from which they depend, can be found in the attached Appendix I.

IV. Status of Amendments (37 C.F.R. § 1.192(c)(4))

As discussed above, Appellants submit herewith, in a separate paper, an Amendment to cancel claims 91-107 from the present application pursuant to MPEP § 1207. Upon entry of this Amendment, claims 75-90 will be pending in the present application ("the pending claims").

V. Summary of the Invention (37 C.F.R. § 1.192(c)(5))

The present invention provides a microlaboratory system that is useful for performing high-throughput screening assays. In particular, the present invention provides microfluidic devices that are useful in screening large numbers of different compounds for their effects on a variety of chemical, and preferably, biochemical systems. Specification, page 7, lines 5-9. In the interest of efficiency, screening assays

have typically been set up in multi-well reaction plates, e.g., multi-well microplates, which allow for the simultaneous, parallel screening of large numbers of test compounds. Specification, page 10, lines 29-32.

An example of a novel system which uses conventional multi-well microplates is shown with respect to Figure 7.

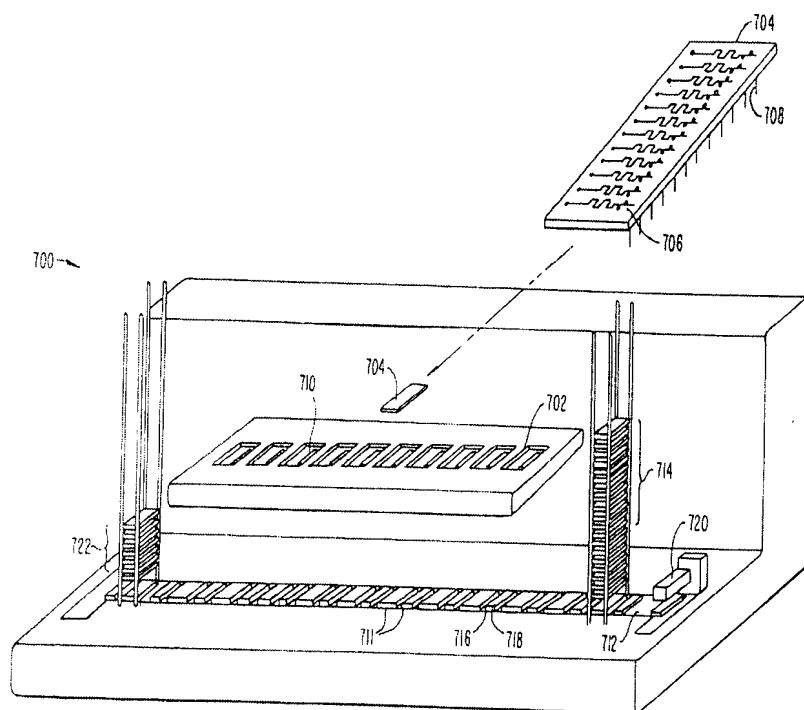


FIG. 7.

A test compound processing system 700 includes a platform 702 which can hold a number of separate assay chips or devices 704. Each chip includes a number of discrete assay channels 706, each channel having a separate interface 708, e.g., a pipettor, for introducing test compounds into the device. These interfaces are used to sip test compounds into the device, separated by sipping spacer fluid and guard band fluids. In the system shown, the interfaces of the chip are inserted through an opening 710 in the bottom of the platform 702, which is capable of being raised and lowered to place the

interfaces in contact with test compounds or wash/spacer/guard band fluids, which are contained in, e.g., multi-well micro plates 711. Specification page 36, lines 1-14; FIG. 7.

The multi-well micro plates 711 are positioned below the platform, e.g., on a conveyor system 712. In operation, multi-well plates containing large numbers of different test compounds are stacked 714 at one end of the conveyor system. The plates are placed upon the conveyor separated by appropriate buffer reservoirs 716 and 718, which may be filled by buffer system 720. The plates are stepped down the conveyor and the test compounds are sampled into the chips, interspersed by appropriate spacer fluids. After loading the test compounds into the chips, the multi-well plates are then collected or stacked 722 at the opposite end of the system. Specification page 36, lines 15-24; FIG. 7.

The devices 704 may be readily attached to a robotic system which allows test compounds to be sampled from a number of multi-well plates that are moved along, e.g., a conveyor system. Specification page 37, lines 9-15; FIG. 7.

VI. Issues (37 C.F.R. § 1.192(c)(6))

The issue on appeal is whether claims 78, 81, and 87 are patentable under 35 U.S.C. § 112, first paragraph. Specifically, whether the subject matter of claims 78, 81, and 87 was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

VII. Grouping of the Claims (37 C.F.R. § 1.192(c)(7))

Claims 78, 81 and 87 should be treated as one group. The claims in this group should stand or fall together. Claim 78, the corresponding dependent claim 81, and

claim 87 relate to the well plate format of the array of sample wells. Specifically, claims 78 and 87 call for the array of sample wells to conform to the format of a 96, 192, 384, or 1536 well plate.

VIII. Argument (37 C.F.R. § 1.192(c)(8))

A. Legal Standard for Written Description

To satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, an Applicant must convey with reasonable clarity to those skilled in the art that, as of the effective filing date, the Applicant was in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). As made clear by the Federal Circuit, "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000).

The Federal Circuit has recently adopted the standard for determining compliance with the written description requirement as set forth in the USPTO's "Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, Written Description Requirement." *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). According to the USPTO's Guidelines:

The analysis of whether the specification complies with the written description requirement calls for the Examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed. *See e.g., Wang Labs. v. Toshiba Corp.*, 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993).

Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. *See e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986).

B. Final Rejection

In the present case, the Examiner rejected claims 78, 81, and 87 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states in the final rejection of the claims under 35 U.S.C. § 112, first paragraph:

The specification discloses an apparatus that include bead resting wells (pg. 28, lines 34-38) and an apparatus that contained multiwell micro plates (pg. 36, line 14; ref. #711 of fig. 7). A method in which test compounds are immobilized on beads in a parallel assay system the parallel channels may be fabricated to include bead resting wells (pg. 28, lines 24-38).

Nowhere in the specification is there a teaching of sample wells that conform to a format of a 96, 192, 384, or 1536 well plate. Additionally in the multiwell micro plates (ref. #711) of fig. 7, the wells are not in a format of a 96 well plate.

Final Office Action (Paper No. 18), mailed February 12, 2003, page 4, lines 1-7.

Additionally, the Examiner states in the final rejection in the "Response to Arguments" made by Appellants:

It is the examiner position that a genus (multiwell microplates) is not descriptive in defining a specific species (96, 192, 384, or 1536 well plates). Further, the six references provided by the applicant to demonstrate that the disclosure of "multiwell microplates" in the specification would provides adequate support for the claims covering 96, 192, 384, or 1536 well plates have been fully considered but they are not persuasive. Because these reference shows that "multiwell plates or

microplates" is further define by a specific format ("96, 192, 384, or 1536 well plates"). For example, Warner et al. (US Patent 5,604,130) states that ". . . *the present invention may be produced for use with a variety of multiwell plate formats including but not limited to 6-wel plates, 12-well plates, 24-well plates, 36-well plates, 48-well plates, 96-well plates, 384-well plates, and the like*" (col. 7, lines 5-9). Therefore, there are no adequate support for claims 78, 81, and 81.

Final Office Action (Paper No. 18), mailed February 12, 2003, page 4, line 20-page 5, line 8 (emphasis in original).

C. The Claimed Invention is More Than Adequately Described in the Specification

Appellants appeal this rejection on the ground that the specification provides adequate written description for the claimed subject matter. Specifically, the specification provides adequate written description for sample wells with the format of a 96, 192, 384, or 1536 well plate.

The specification of the present invention describes a microlaboratory system that is useful for performing high-throughput screening assays. In particular, the present invention provides microfluidic devices that are useful in screening large numbers of different compounds for their effects on a variety of chemical, and preferably, biochemical systems. Specification, page 7, lines 5-9. The specification notes that in the interest of efficiency, screening assays have typically been set up in multi-well reaction plates, e.g., multi-well microplates, which allow for the simultaneous, parallel screening of large numbers of test compounds. Specification, page 10, lines 29-32. The microfluidic assay chips (704) of the present invention include a plurality of interfaces (708), e.g., pipettors, that lower into the array of sample wells of a plurality of *multi-well* microplates (711) (emphasis added). Specification p. 36, lines 1-14; FIG. 7.

In this way, the specification of the present invention discloses multi-well microplates that are used in a system that screens *large numbers* of compounds. This description clearly satisfies the written description requirement for a *multi-well* microplate. The Examiner states that the written description requirement for the feature calling for sample wells that conform to a format of a 96, 192, 384, or 1536 well plate is not satisfied because the written description does not teach such specific formats. See Final Office Action (Paper No. 18), mailed February 12, 2003, page 4, lines 1-7.

First, the written description requirement does not require the applicant "to describe exactly the subject matter claimed." See *Union Oil Co.*, 208 F.3d at 997. Rather, the Applicant must simply convey with reasonable clarity to those skilled in the art that as of the effective filing date, the Applicant had possession of the invention. See *Vas-Cath*, 935 F.2d at 1555. Next, information which is well known in the art at the time the invention was made need *not* be described in detail in the specification. See *Hybritech*, 802 F.2d at 1379. Additionally, when the level of skill in the art for a claimed feature is high, the extent of disclosure necessary to satisfy the written description requirement is low. See *id.*

The specific well plate formats called for in claims 78 and 87 were well known in the art as of the effective filing date of the application, i.e., June 28, 1996. Specifically, many patents filed prior to the effective filing date of the present application disclose these standard well plate arrangements and evidence that such configurations were well known in the art at the time. In particular, U.S. Pat. No. 5,508,005, col. 7, lines 14-19; Filed Oct. 26, 1993 (stating "the present invention may comprise a variety of configurations. For example, 6-well, 12-well, 24-well, 48-well, 96-well, and 192-well configurations may be fabricated."); U.S. Pat. No. 5,604,130, col. 7, lines 5-9; Filed May

31, 1995 (stating "the present invention may be produced for use with a variety of multiwell plate formats, including but not limited to 6-well plates, 12-well plates, 24-well plates, 36-well plates, 48-well plates, 96-well plates, 384-well plates, and the like."); U.S. Pat. No. 5,560,811, col. 11, lines 31-35; Filed Mar. 21, 1995 (stating "Those skilled in the art will recognize that the above liquid handling system provides for simultaneous and quantitative sampling of a large array of samples by sipping from the 96, 192, or 384-well plates or arrays of microtubes with an array of sipper capillaries."); U.S. Pat. No. 5,753,511, col. 10, lines 20-22 (stating "The test plate can be made from any suitable material and can have any number of wells, such as 6, 24, 96 or 384 wells."); U.S. Pat. No. 6,100,026, col. 9, lines 62-67; Filed June 10, 1996 (stating "For example, microplates, such as a microtiter . . . or other such high density format 196, 384 1536 or more wells per plate . . ."); U.S. Pat. No. 6,319,668, col. 7, lines 49-51; Filed June 24, 1996 (stating ". . . is particularly suited for application to each well in a microplate, such as a microtiter plate, that contain 96, 384, 1536 or higher density formats.").

By describing the present invention as using a plurality of *multi-well* microplates, and realizing that the specific well plate formats called for in claims 78 and 87 were well known in the art, Appellants convey with reasonable clarity to those skilled in the art that as of the time of their effective filing date, the Appellants had possession of the claimed invention. In this way, the written description requirement of 35 U.S.C. § 112, first paragraph is satisfied for claims 78, 81, and 87.


IX. Conclusion

The subject matter of claims 78, 81, and 87 is patentable because the written description requirement for these claims has been satisfied. Therefore, Appellants

respectfully request that the Board reverse the Examiner's final rejection of these claims under 35 U.S.C. § 112, first paragraph, and remand this application for an interference.

Respectfully submitted,

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Appendix I

76. An apparatus for conducting a microfluidic process, said apparatus comprising:

(a) a first plate comprising an array of sample access ports adapted for receiving a plurality of samples from an array of sample wells; and,

(b) a second plate integral with said first plate, said second plate comprising a planar array of microfluidic networks of cavity structures and channels for conducting a microfluidic process wherein each of said microfluidic networks is adapted for fluid communication with a corresponding sample access port of said first plate.

78. The apparatus of claim 76, wherein said array of sample wells conforms to the format of a 96, 192, 384, or 1536 well plate.

81. The apparatus of claim 78, wherein each of said microfluidic networks of cavity structures and channels comprises a tortuous path.

83. A method for processing an array of samples, said method comprising:

(a) simultaneously transferring at least a portion of each sample in an array of sample wells to a corresponding array of sample access ports that are part of a first plate comprising an array of sample access ports adapted for receiving a plurality of samples from an array of sample wells,

(b) simultaneously transferring at least a portion of each sample from said sample access ports to a corresponding array of microfluidic networks that is a part of a second plate integral with said first plate, said second plate comprising a planar array of

microfluidic networks of cavity structures and channels for conducting a microfluidic process wherein each of said microfluidic networks is adapted for fluid communication with a corresponding sample access port, and

- (c) processing said array of samples.

87. The method of claim 83, wherein said array of sample wells conforms to the format of a 96, 192, 384, or 1536 well plate.